REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Initially, Applicants wish to thank the Examiner for his courtesy and helpful comments provided to their representatives during the personal interview. Applicants have amended the claims along the lines suggested by the Examiner during the interview.

I. CLAIM STATUS AND AMENDMENTS

Claims 3, 6 and 8 were pending in this application when last examined.

Claim 3 is amended to help better define the composition as suggested by the Examiner. Thus, claim 3 is amended to recite that the prolonged-release fraction contains an excipient of matricial type. Support for this limitation can be found on page 8, lines 31-34, of the specification as filed. Claim 3 is further amended to recite that the immediate-release fraction contains an excipient selected from diluents, binders, disintegrating agents, lubricants and flow enhancers, taste-masking agents, flavorings and colorants. Support for this limitation can be found on page 10, lines 7-17, of the specification as filed. Claim 3 is also slightly amended to recite "is ~~administered as~~ a single daily dose".

Claim 9 is newly added and is directed towards a weight ratio of efletirizine in the immediate-release fraction to the prolonged-release fraction of between 1.6 and 0.05. Support for claim 9 can be found on page 13, lines 7-11, of the specification as filed.

Claim 10 is newly added and is directed towards the prolonged-release fraction containing specified excipients and the immediate-release fraction also containing specified excipients. Support for this claim can be found in table 15 on page 26 of the specification as filed.

No new matter has been added.

II. DECLARATION UNDER 37 CFR 1.132

On page 3 of the Office Action of April 19, 2007, the Office indicated that the Declaration submitted under 37 CFR 1.132 on February 23, 2007 was deficient because it did not

compare the invention to the closest prior art. In particular, the Office contended that the closest prior art would be the art-known immediate release formulation. Applicants respectfully note that the Declaration compared 60 mg immediate release efletirizine capsules to the claimed pharmaceutical composition. Applicants note that this composition is an art-known immediate release formulation. Therefore, applicants respectfully request the Examiner to reconsider the Declaration under 37 CFR 1.132 submitted on February 23, 2007 in light of the claims as amended since such Declaration does compare the closest prior art to the claimed pharmaceutical formulation. During the interview, it is believed that the Examiner did agree with Applicant's position.

III. OBVIOUSNESS REJECTIONS

On pages 2-3 of the Office Action of April 19, 2007, claim 3 was rejected under 35 U.S.C. § 103(a) as obvious over Sunshine et al. in view of Kreutner et al. Claim 8 was also included in this rejection.

On page 5 of the Office Action, claim 6 remained rejected under 35 USC § 103 as obvious over Sunshine et al. in view of Kreutner et al. and further in view of Guy et al.

Applicants respectfully traverse the rejections for the reasons of record and for the following reasons.

During the interview, the Examiner suggested adding further limitations to the claims. In this regard, Applicants respectfully note that claim 3 recites that the weight ratio of efletirizine in the immediate-released fraction to the prolonged-release fraction is between 3 and 0.025. Applicants further note that claim 3 recites that the amount of efletirizine in the pharmaceutical composition is between 10 and 70 mg.

The Examiner also suggested Applicants include limitations directed towards the excipients in the various tablet portions. Applicants have therefore amended claim 3 to require that the prolonged-release fraction contain an excipient of matricial type and the immediate-released fraction contain an excipient chosen from a specified group. Applicants have also enclosed a graph with this Preliminary Amendment illustrating the amounts of efletirizine in each fraction (Attachment A).

Applicants further note that the claims, as amended, are directed toward a combination of an immediate-release efletirizine fraction and a prolonged-release efletirizine fraction with specified excipients in each fraction. The amount of efletirizine in each fraction is limited to the particular ratios and mathematical formulas given in claim 3. Further, the total amount of efletirizine is limited to 10-70 mg. These limitations on the amount of efletirizine in claim 3, as amended, make it possible to satisfy the specific pharmacokinetic requirements related to the use of efletirizine as a single daily dose and minimize variations in bioavailability and maximum plasma concentrations associated with having a meal just prior to ingestion of the pharmaceutical. This unexpected and inherent property of the claimed invention is shown in Example 5 on page 22 of the specification. This property is not observed for immediate-release compositions as demonstrated in Example 4 on page 20 of the specification. Furthermore, this property of the claimed pharmaceutical composition is surprising and unexpected as indicated by the 37 C.F.R. § 1.132 Declaration submitted February 23, 2007. As a result of this inherent property, the consequences of incorrect handling or use by a patient of the claimed composition are reduced.

Applicants also note that claim 3 is amended to recite that the claimed composition "is a single daily dose". Applicants therefore suggest that such a limitation should be given patentable weight. In particular, after intense research, the present inventors have found the limits and equations recited in claim 3 for the amounts of efletirizine in each fraction express the necessary balance between immediate release of the active principle and prolonged release of the active principle for maintaining an effective dose of the active principle for a full day while avoiding reaching plasma concentration peaks associated with side effects.

Finally, Applicants note that a skilled artisan could not look to the literature and effectively compare efletirizine with other antihistamines such as loratadine and cetirizine, due to efletirizine's very specific pharmacokinetic characteristics (including half-life, plasmatic elimination, oral clearance, etc.) For example, loratadine is a long acting drug exhibiting a dose-related rapid onset inhibition of the histamine-induced skin wheal and flare response in humans. Loratadine is apparent in the plasma 2 hours after ingestion and persists throughout the 24 hour observation period. The loratadine elimination half-life (t 1/2b) ranges from 7.8 to 11 hours;

the descarboethoxyloratadine half-life ranges from 17 to 24 hours; and the cetirizine half-life ranges from 6.5 to 10 hours. Thus, these antihistamines already possess pharmacokinetic characteristics suitable for single daily doses and a skilled artisan would not examine such literature for obtaining single daily dose pharmaceuticals containing principals with significantly shorter half-lives such as efletirizine, which has a half-life of 2.5 to 3.5 hours.

Efletirizine, unlike loratadine, does not persist throughout the 24-hour observation period. Consequently, a very specific galenic composition is required to obtain a single daily dose tablet. Moreover, due to the pharmacokinetic characteristics of loratadine, a skilled artisan cannot merely replace loratidine with efletirizine in a galenic composition containing loratadine as an active ingredient and obtain a similar pharmacokinetic profile.

Thus, Applicants submit that the cited references do not teach or suggest to a person of skill in the art the very specific relationship between the prolonged-release and the immediate-release fraction recited in claim 3 that results in a single daily dose with suitable pharmacokinetics that is resistance to variations in bioavailability and maximum plasma concentrations associated with having a meal just prior to ingestion of the pharmaceutical.

Applicants therefore respectfully suggest that neither Sunshine et al. in view of Kreutner et al. nor Sunshine et al. in view of Kreutner et al. and further in view of Guy et al. teach or suggest the claimed single daily dose efletirizine composition with the unexpected inherent property of resistance to variation in bioavailability and maximum plasma concentration of the active principle caused by ingestion of a meal prior to ingestion of the claimed pharmaceutical composition. Furthermore, none of the cited references teach or suggest that a principal with a short half life, such as efletirizine, can be used as a single daily dose tablet that maintains an effective dose of the active principle for a full day while avoiding reaching plasma concentration peaks associated with side effects. Applicants therefore respectfully suggest that these rejections, as applied to the amended claims, are untenable and should be withdrawn.

CONCLUSION

In view of the forgoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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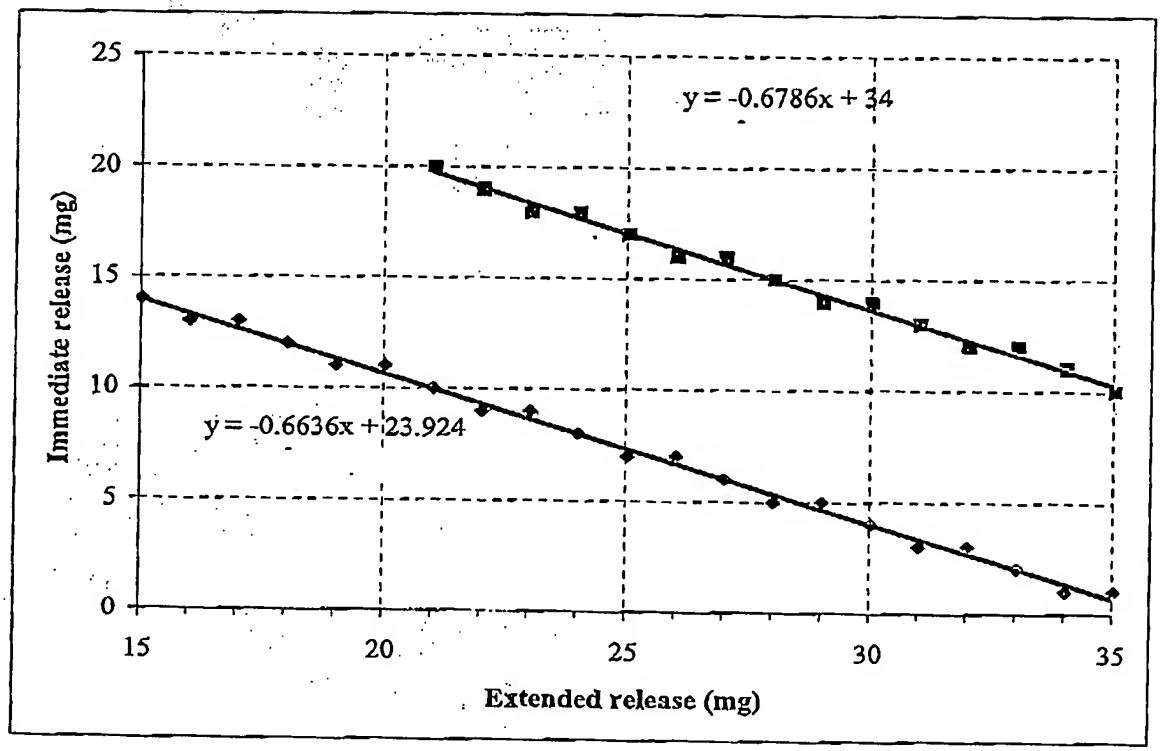

ATTACHMENT A